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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,146	09/16/2002	Wilhelm Amberg	51748	9829

32116 7590 07/26/2006

WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,146	AMBERG ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-10* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/11/06 has been entered.

2. Claims 1-4 and 7-10 are pending.

3. Claims 1-3 and 7-9 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 4 and 10 are under examination as they read on an a pharmaceutical composition for the treatment or prevention of cardiovascular diseases comprising an ET_A endothelin blocker and an $\alpha v\beta 3$ integrin receptor antagonist and a trade package thereof.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 4 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Kirchengast *et al* (provided in the International Report and cited on the PTO-892 as reference Y) in view of Srivatsa *et al* (provided in the International Report and cited on the PTO-892 as reference W) for the same reasons set forth in the previous Office Actions mailed 2/28/05 and 1/11/06.

Applicant's arguments, filed 5/11/06, have been fully considered, but have not been found convincing.

Applicant traverses the rejection on the basis that the specifically claimed combination is not taught and it leads to a surprising effect. Applicant submits that the present invention permits the

use of each component at a dose less than the dose useful alone, with a reduction in side effects (page 4, lines 23-27 and page 20, lines 24-30). Furthermore there is no prior art cited and applied to support the proposition relied upon that coadministration of an endothelin blocker and αvβ3 integrin antagonist is expected to provide efficacy at lower doses than the doses used individually, with reduction in side effects.

However, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See MPEP 2144.06. The suggestion to combine each of the two components of the claimed composition is conventionally employed in the art for treating restenosis come within the purview of combining two or more materials where each is taught by the prior art to be useful for the same purpose. It would have been *prima facie* obvious, within the meaning of 35 U.S.C. 103 to employ these components in combination for their known functions and to optimize the amount of each additive.

Regarding the surprising effect of the claimed combination, the issue is whether the properties differ to such an extent that the difference is really surprising. These effects are not surprising because co-administer ET_A endothelin blocker and αvβ3 integrin receptor antagonist is expected to provide efficacy at lower doses than the doses useful individually, with a reduction in side effects. Combination therapy is used to minimize dose-dependent side effects of an individual drug. In order for the claimed combination to be surprising there must be some form of synergy (i.e., resulting in an effect greater than the sum of the several effects taken separately) or unexpected effect. However, Applicant provides combination therapy with drugs that permits the use of each component at a dose less than the dose useful alone, with a reduction in side effects, which is an expected efficacy in the resultant combination.

Regarding lack of prior art citation to support the Examiner's position, the examiner notes an evidentiary reference to support the Examiner's position is not required to be prior art but can be post dated reference. The Examiner draws Applicant's attention to U.S. 20060089374, which teaches that combination therapy, **in general**, supports appropriate level dosing in that it allows the application of doses of individual agents lower than those that elicit the unwanted side effects that may occur at higher dose levels. Further, in the case of combining agents that work toward a broadly defined common benefit but which operate through different mechanisms of action, synergistic therapeutic effects may occur. Synergistic effects, by their nature, are not commonly predictable, based solely on an understanding of the mechanisms of the combined individual agents, respectively (see paragraph 32 in particular).

7. Claim 10 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Kirchengast *et al* (provided in the International Report and cited on the PTO-892 as reference Y) in view of Srivatsa *et al* (provided in the International Report and cited on the PTO-892 as reference W) as

applied to claims 4-6 above, and further in view of US Pat. No. 4,761,406 for the same reasons set forth in the previous Office Actions mailed 2/28/05 and 1/11/06.

Applicant's arguments, filed 5/11/06, have been fully considered, but have not been found convincing.

Applicant traverses the rejection base on the same reasons set forth above.

The Examiner's position is the same as set forth above.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 24, 2006

Maher Haddad

Maher Haddad, Ph.D.
Primary Examiner
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